PATENT SPECIFICATION

1,010,998

NO DRAWINGS

Inventor: PETER MICHAEL BLANCHARD

Date of filing Complete Specification: Sept. 13, 1963.

Application Date: Oct. 9, 1962. No. 38167/62.

Complete Specification Published: Nov. 24, 1965.

Index at acceptance:—C2 C(2A3, 2A9, 2B3A4, 2B3B, 2B3G4, 2R18)

Int. Cl.:—C 07 d

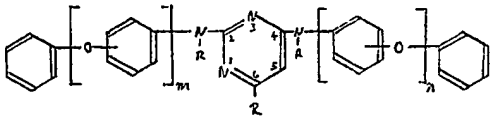
COMPLETE SPECIFICATION

Pyrimidine Derivatives

We, THE BRITISH PETROLEUM COMPANY LIMITED, of Britannic House, Finsbury Circus, London, E.C.2, a British joint-stock Corporation, and PETER MICHAEL BLANCHARD, of the Company's Research Centre, Chertsey Road, Sunbury-on-Thames, Middlesex and of British nationality, do hereby declare the invention for which we pray that a patent may be granted to us, and the method by which it is to be performed to be particularly described in and by the following statement:—

This invention relates to pyrimidine derivatives having utiltiy as thermally stable materials, and, in some cases, as high temperature lubricants.

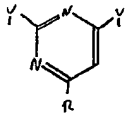
The invention consists in new compounds of the general formula:



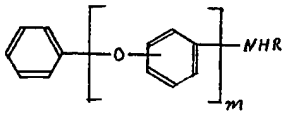
(Formula I)

where the Rs are hydrogen or an alkyl group having 1—4 carbon atoms, e.g. methyl, not necessarily the same at each occurrence, and m and n are each 0, 1 or 2.

The invention also comprises a two-stage method of preparing compounds of the general formula I in which the first stage comprises reaction, at a temperature low enough to allow reaction to take place to give a monosubstituted product, between a 2:4-dihalopyrimidine of the general formula:—



and an aromatic amino-compound of the general formula:—



where:—

R and m have the values specified above

Y is chlorine or bromine,

whereby the halogen in the 2-position is substituted, and the second stage comprises reaction at elevated temperature between the mono-halo compounds so formed and the same or a different aromatic amino-compound of the formula specified above whereby the other halogen atom is substituted, both stages being carried out in the presence of a base which removes the acid HY which is formed, e.g. caustic soda or excess of the amino-compound.

[Price 4s/6d.]

We have found that a high temperature during the first stage tends to encourage the formation of disubstituted compounds. On the other hand a lower temperature gives a less vigorous reaction which favours the reaction with the halogen substituent in the more active 2-position and thereby favours the production of monosubstituted products (the temperature should not, of course, be reduced to such an extent that the reaction is stopped altogether).

Preferably the first stage is carried out in solution in an inert solvent, e.g. ethanol, and preferably the molar amount of the aromatic amino-compound is equivalent to the molar amount of the 2:4-dihalopyrimidine. Conveniently the first stage is carried out at 0°C.—15°C., e.g. by leaving the reactants on ice until the reaction is complete.

The second stage is preferably carried out by refluxing a solution of the reactants in an inert volatile solvent, e.g. di-ethyl carbitol. In the second stage the molar amount of the aromatic amino compound should preferably be at least equal to the molar amount of the other reactant.

Alternatively, where it is desired to prepare compounds of formula I having the same substituent group in both the 2- and 4-positions on the pyrimidine ring, the reaction may be carried out in a single stage using conditions similar to those described for the second stage referred to above. When carrying out the reaction in this way, the molar amount of the amino compound should preferably be at least twice the molar amount of pyrimidine compound.

The single stage method may also be used to prepare mixed compounds of formula I by using more than one amino compound in the reaction, the product of the reaction being a statistical mixture of molecules of formula I.

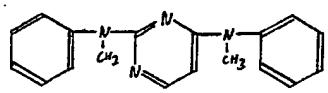
The 2:4-dihalopyrimidine may be prepared by halogenating uracil (2:4-dihydroxy pyrimidine) e.g. by refluxing uracil with phosphoryl chloride, pouring the mixture on ice and extracting the required product with ether. 2:4-dichloro-6-methyl-pyrimidine may be similarly prepared from methyl uracil (2:4-dihydroxy-6-methyl-pyrimidine).

If necessary, the uracil may be prepared very simply by the method of Baudisch and Davidson by condensing malic acid and urea in oleum and diluting with water to precipitate the uracil which may be filtered off and recrystallised if necessary. Methyl uracil may be prepared by condensing ethyl acetoacetate and urea and warming the crystalline product with concentrated caustic soda to produce the methyl uracil which may be filtered off after suitable dilution and acidification, and recrystallised if necessary.

A number of examples of the invention will now be described.

EXAMPLE 1.

2:4-Bis(N-methylanilino) pyrimidine, a compound of the formula



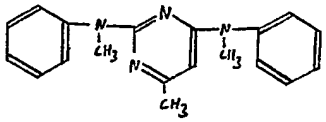
(Formula III)

was prepared as follows

10 gm (ca 0.07M) of 2:4-dichloropyrimidine was refluxed with 39 gm (ca 0.36M) of N-methylaniline for 4 hours. At the end of this period, the viscous reaction mixture was cooled and poured into water, thoroughly washed and extracted with ether. After removing the ether, the residue was distilled under vacuum giving 16 gm of the above product.

EXAMPLE 2.

Example 1 was repeated on an 0.05M scale using 2:4-dichloro-6-methyl pyrimidine instead of 2:4-dichloropyrimidine. The final product was 2:4-bis(N-methyl-anilino)-6-methyl pyrimidine i.e. a compound of the formula

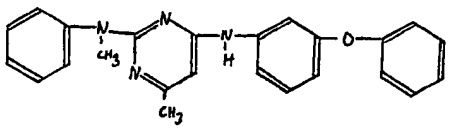


(Formula IV)

The yield was 10 gm.

EXAMPLE 3.

A compound of the formula



(Formula V)

was prepared on an 0.05M scale using a two-stage reaction. In the first stage the 2:4-dichloro-6-methylpyrimidine was dissolved in ethanol and stood on ice and an equimolar amount of N-methylaniline was added together with sufficient caustic soda to remove the HCl formed during the reaction. The mixture was left on the ice at a temperature between 0°C. and room temperature for 24 hours after which the sodium chloride formed was filtered off and the filtrate distilled to give the colourless, intermediate 2-N-methylanilino-4-chloropyrimidine. This compound was then refluxed with a slight molar excess of meta-phenoxy-N-methylaniline and sufficient caustic soda in diethylcarbitol for 6 hours. The sodium chloride formed was filtered off as before and the final product was recovered by distillation under vacuum. The yield was 15 gm.

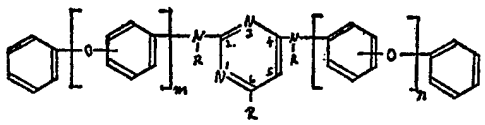
The properties of the products of the examples are given in the following Table.

TABLE

Formula	III	IV	V
Boiling Point : °C	182/0.5 mm	182/0.8 mm	210/0.1 mm
Pour Point : °F	50	55	—
n_D^{20}	1.6496	—	—
Colour & form	Pale yellow solid	Pale yellow solid	Pale yellow viscous liquid
Viscosity	—	—	34.7 cc at 210°F

WHAT WE CLAIM IS:—

1. Chemical compounds of the general formula:—



where:—

R is hydrogen or an alkyl group having 1—4 carbon atoms, and m and n are each 0, 1 or 2.

2. Compounds according to claim 1, in which R is hydrogen.

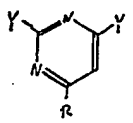
3. Compounds according to claim 1, in which R is methyl.

4. Compounds according to any one of the preceding claims, in which n=m=0.

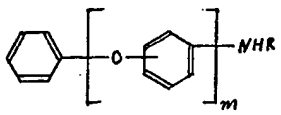
5. Compounds according to any one of claims 1—3, in which n=1 and m=0.

6. Compounds having any one of the formulae III, IV or V as given in the body of the specification.

7. A two-stage method of preparing a compound as specified in any one of the preceding claims, in which the first stage comprises reaction, at a temperature low enough to allow reaction to take place to give a monosubstituted product, between a 2:4-dihalopyrimidine of the general formula:—



and an aromatic amino-compound of the general formula:—



where:—

R and m have the values specified in claim 1—5,

Y is chlorine or bromine,

whereby the halogen atom in the 2-position is substituted, and the second stage comprises reaction at elevated temperature between the mono-halo compound so formed and the same or a different aromatic amino-compound of the formula specified above whereby the other halogen atom is substituted, both stages being carried out in the presence of a base which removes the acid HY which is formed.

8. A method according to claim 7, in which the first stage of the reaction is carried in solution in an inert solvent.

9. A method according to claim 8, in which the inert solvent is ethanol.

10. A method according to any one of claims 7—9, in which the second stage of the reaction is carried out by refluxing a solution of the reactants in an inert volatile solvent.

11. A method according to claim 10, in which the inert volatile solvent is diethyl carbitol.

12. A method according to any one of claims 7—11, in which the first stage of the reaction is carried out at 0°—15°C.

13. A method of preparing compounds as specified in any one of claims 1—6, in which a 2:4-dihalopyrimidine and one or more aromatic amino-compounds, all as specified in claim 7, are dissolved in an inert volatile solvent and the solution refluxed, in the presence of a base which removes the acid HY which is formed, until the reaction is complete.

14. A method according to claim 13 in which the inert solvent is diethyl carbitol.

15. A method according to any one of claims 7—14, in which the base is caustic soda.

16. A method according to any one of claims 7—14, in which the base is an excess of the aromatic amino-compound.

17. A method of preparing a compound as claimed in claim 1, as hereinbefore described with reference to any one of the examples.

18. A compound as claimed in claim 1, prepared by a reaction according to any one of claims 7—17.

J. WOOLARD,
Agent for the Applicants,
Chartered Patent Agent.

Leamington Spa: Printed for Her Majesty's Stationery Office, by the Courier Press (Leamington) Ltd.—1965. Published by The Patent Office, 25 Southampton Buildings, London, W.C.2, from which copies may be obtained.